

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

ELSEVIER

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation



TDCS in a patient with dreadlocks: Improvements in COVID-19 related verbal fluency dysfunction



To the Editor

The enduring neuropsychological impacts of COVID-19, termed PASC (post-acute sequelae SARS-CoV-2 infection), remain poorly understood. Transcranial direct current stimulation (tDCS) is an appealing treatment for PASC because of the tolerability and feasibility of home use and emerging evidence for efficacy [1]. Here we describe a person with PASC presenting with speech and language dysfluency, a symptom responsive to frontal tDCS treatment [2]. To the best of our knowledge, this is the first demonstration that tDCS remediates acquired dysfluency following severe SARS-CoV-2 infection.

The patient was a 63 year-old Veteran of African and Native American descent who recovered from severe COVID-19, presented with markedly dysfluent speech, and wore dreadlocks. He reported a developmental history of "stuttering" that resolved by high school. He graduated from an elite college with a degree in electrical engineering and worked as a network operations manager. In January 2021, he was hospitalized with severe COVID-19. Seven months later, speech pathology assessment (see Supplement Table 1 for detailed language testing results) revealed marked dysfluency in spontaneous speech. Given his education, verbal fluency should have been in the high average range but was instead low average on a word list generation measure [3]. He was referred to our larger study of COVID-related stress that provided combined psychotherapy and tDCS of the frontal lobes during guided relaxation (Supplement to NCT03851380). African Americans with dreadlocks or cornrows are commonly excluded from tDCS studies due to concerns that consistent electrode contact with the scalp may not be reliable and that hair oil treatments or the thick, braided, hair may cause excessive electrode movement that may change current delivered by tDCS to the brain [4]. However, we knew of no empirical evidence that such hairstyles necessarily interfere with tDCS outcomes and enrolled him after obtaining informed consent. A clinical MRI from immediately before therapy revealed only a small lesion on diffusion weighted imaging in the anterior insula.

He self-administered a total of 30 tDCS sessions from home with a battery driven, constant current stimulator (REMOTE Mini-CT, Soterix Medical, NY), and disposable, premoistened, saline-soaked sponge electrodes (5×5 cm). Stimulation occurred twice daily over 3 weeks (2 mA, 30 minutes duration with 30 seconds ramp-up/ramp-down) with a bifrontal montage positioned with a SNAP-strap (Soterix Medical). The anode targeted the left dorsolateral prefrontal cortex (DLPFC) and the cathode the right DLPFC (F3 and F4 according to the 10-20 EEG system), slightly adapted to accommodate the patient's dreadlocks (see Fig. 1a). For the first

two weeks the patient received stimulation with electrodes at the hairline, half on the forehead and half on the scalp over the dreadlocks (but close to F3/F4), during which time the patient cleaned the underlying scalp area with saline prior to sessions to improve contact and reduce the potential interference of oil-based hair products (montage 1). Continuous monitoring of electrode contact quality using montage 1 revealed adequate contact for 99.7% of treatment and poor contact for only one session for a total of 5 seconds. For the third (final) week he moved the montage just anterior to the hairline so the entire electrode made skin contact; the electrodes were thus farther from F3/F4 but the stimulation was unaffected by the dreadlocks, and no instances of poor contact quality were recorded (montage 2). Fig. 1a displays the electric field maps for montage 1 and montage 2 [5]. Beginning after the second to last treatment, the patient developed skin irritation and swelling under the anode near the eye (no lesions), which resolved after the last treatment, about a day later. Skin irritation has been previously reported in about 3.3% of subjects undergoing tDCS, typically developing after 4-5 sessions [6]. We doubt that our patient's skin irritation was related to the dreadlocks, because no irritation occurred during the first two weeks of treatment when stimulation was delivered over the dreadlocks, but only occurred after a week after delivery exclusively on the forehead. Therapy course was otherwise uncomplicated, with the patient reporting occasional sleepiness post-stimulation, but no other unexpected side effects (See Supplement: Observation and Reporting of Side Effects).

The electric field map of Fig. 1b reveals maximal modulation in inferior frontal areas 44, 45, 47, IFJa, and IFSp [[7], p.73], which partially overlaps with the language network white matter tracts derived using O8t (Omniscient Neurotechnologies). Verbal fluency markedly improved after tDCS. To reduce practice effects, validated parallel test forms were used. Whereas a healthy cohort produces on average fewer than one more word on second testing [3], our patient produced nine more words for phonemic (letter) cues, ten more for semantic (category) cues, and two more in the switching condition (switching between two categories). Fig. 1c displays the magnitude of this improvement in terms of the patient's agecorrected scaled scores relative to a normative cohort (mean = 10, standard deviation = 3), illustrating increases of aboutone standard deviation from pre to post stimulation for all subtests and final performance in the average to high average range. Our improvements are consistent with a prior study of anodal left DLPFC stimulation in healthy participants [8] who showed improvements in both phonemic and semantic fluency, using a cathode positioned over the right shoulder. Modeling of semantic and phonemic similarity of the patient's wordlists suggest search strategy changes

A.C. Rosen, J.A. Lavacot, I.M. Porter et al.

Brain Stimulation 15 (2022) 254–256

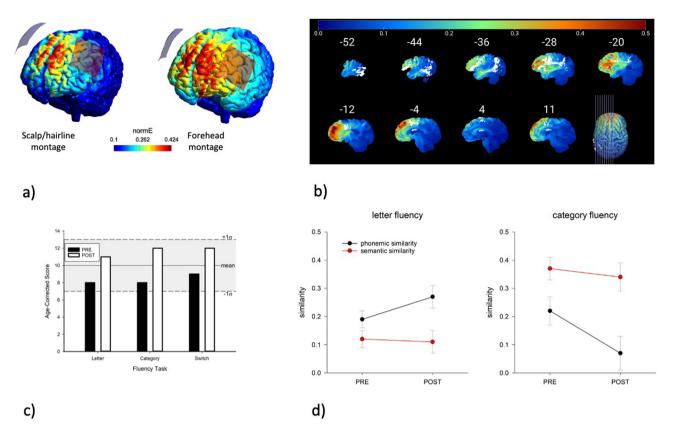


Fig. 1. a) The norm of the electric field generated by the electrode montages on the subject's brain surface, with the electrode (gray square) positions shown. Electric fields were generated using SimNIBS 3.2. b) The norm of the electric field throughout the brain volume is shown, with the white matter tracts of the language network (derived using O8t, Omniscient Neurotechnologies) overlaid in white. c) D-KEFS scores before (PRE) and after (POST) tDCS treatment; d) Semantic and phonemic similarity scores in the letter cue and category cue conditions, PRE and POST treatment. Error bars denote standard errors of the similarity score model estimates derived from the patient's consecutive responses.

with therapy. Semantic similarity was assessed using GloVe [9] and phonemic similarity was based on edit distance. Results indicated reliance on phonemic similarity increased during the letter cues (Fig. 1d, p = 0.037 and decreased during fluency to category fluency cues (Fig. 1d, p = 0.028).

In summary, we believe this is the first reported case of tDCS therapy improving COVID-related speech/language dysfunction. Modeling of fluency items suggested that frontal stimulation enabled more flexible use of phonemic search to promote lexical access. Further studies that monitor electrode contact quality and outcomes are needed to evaluate whether the electrode positioning adjustments we made impact treatment success in patients with dreadlocks. Provided proper equipment is used, tDCS can be successfully applied in individuals with dreadlocks without requiring hairstyle changes. This removes a barrier to tDCS treatment acceptance in the African American population that has been disproportionately affected by COVID-19 [10], and supports using tDCS to support recovery from PASC.

Declaration of competing interest

Dr. Rosen, Mr. Lavacot, Mr. Porter, Dr. Chao, Dr. Kumar, and Dr. Cardenas have no conflict to disclose. The City University of New York holds patents on brain stimulation with Dr. Bikson as inventor. Dr. Bikson has equity in Soterix Medical Inc. Dr. Bikson consults, received grants, assigned inventions, and/or serves on the Scientific Advisory Boards of SafeToddles, Boston Scientific, GlaxoSmithKline, Biovisics, Mecta, Lumenis, Halo Neuroscience, Google-X, i-Lumen, Humm, Allergan (Abbvie), Apple.

Acknowledgements

This work was supported by a Merit Award #RX003152 and supplement to support research on COVID-19 from the United States (U.S.) Department of Veterans Affairs, Office of Research and Development.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2022.01.004.

References

- [1] Pilloni G, Bikson M, Badran BW, George MS, Kautz SA, Okano AH, et al. Update on the use of transcranial electrical brain stimulation to manage acute and chronic COVID-19 symptoms. Front Hum Neurosci 2020;14(493).
- [2] Busan P, Moret B, Masina F, Del Ben G, Campana G. Speech fluency improvement in developmental stuttering using non-invasive brain stimulation: insights from available evidence. Front Hum Neurosci 2021:15.
- [3] Delis D, Kaplan E, Kramer J. Delis-kaplan executive function system (D-KEFS). San Antonio, TX: The Psychological Corporation; 2003.
- [4] Woods AJ, Bryant V, Sacchetti D, Gervits F, Hamilton R. Effects of electrode drift in transcranial direct current stimulation. Brain stimul 2015;8(3):515–9.
- [5] Saturnino GB, Puonti O, Nielsen JD, Antonenko D, Madsen KH, Thielscher A. SimNIBS 2.1: a comprehensive pipeline for individualized electric field modelling for transcranial brain stimulation. In: Makarov S, Horner M, Noetscher G, editors. Brain and human body modeling: computational human modeling at EMBC 2018; 2019. p. 3–25. Cham (CH).
- [6] Antal A, Alekseichuk I, Bikson M, Brockmöller J, Brunoni AR, Chen R, et al. Low intensity transcranial electric stimulation: safety, ethical, legal regulatory and application guidelines. Clin Neurophysiol 2017;128(9):1774–809.

- [7] Glasser MF, Coalson TS, Robinson EC, Hacker CD, Harwell J, Yacoub E, et al. A multi-modal parcellation of human cerebral cortex. Nature 2016;536:171–8.
- [8] Ghanavati E, Salehinejad MA, Nejati V, Nitsche MA. Differential role of prefrontal, temporal and parietal cortices in verbal and figural fluency: implications for the supramodal contribution of executive functions. Sci Rep 2019;9(1):3700.
- [9] Pennington J, Socher R, Manning CD. Glove: global vectors for word representation. Empir Methods Nat Lang Process 2014:1532–43.
- [10] Yancy CW. COVID-19 and african Americans. JAMA 2020;323(19):1891–2.

Allyson C. Rosen*

Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA

Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA, USA

James A. Lavacot, Ivan M. Porter

Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA

Steven Z. Chao

Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA

Department of Neurology, Stanford University School of Medicine, Stanford, CA, USA

Marom Bikson

Department of Biomedical Engineering. The City College of New York, NY. USA

Abhilasha A. Kumar

Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA

Valerie A. Cardenas

Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA

* Corresponding author. 3801 Miranda Ave (151Y), Palo Alto, CA, 94304-1207, USA.

E-mail address: rosena@stanford.edu (A.C. Rosen).

13 December 2021

Available online 8 January 2022